

Aquaporin Water Channels: The Nobel Lecture presented on December 8, 2003

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Abstract:

A verbatim quote from the Nobel Laureate's Introduction in his Nobel Lecture presented on December 8, 2003: ===== "I am going to talk about aquaporin water channels. We have studied these proteins for several years, and we now understand that they explain how water crosses biological membranes. Water is commonly regarded as the "solvent of life", since our bodies are 70 percent water. All other vertebrates, invertebrates, microbes, and plants are also primarily water. The organization of water within biological compartments is fundamental to life, and the aquaporins serve as the plumbing systems for cells. Aquaporins explain how our brains secrete and absorb spinal fluid, how we can generate aqueous humor within our eyes, how we can secrete tears, saliva, sweat, and bile, and how our kidneys can concentrate urine so effectively. These proteins are fundamental to mammalian physiology, but they are also very important in the lives of microorganisms and plants." ===== "DISCOVERY OF AQP1: The field was essentially stuck, but following the well known scientific approach known as "sheer blind luck", we stumbled upon the protein that is the answer to the question: do water channels exist? Looking through our notebooks for the earliest studies that showed there was such a protein, I found an autoradiograph prepared by my first lab assistant, Andy Asimos. Nevertheless, none was functionally defined. These clues heightened our suspicion that the 28 kDa protein was a water transporter, so we tested for possible water transport function in collaboration with our colleague Bill Guggino at Johns Hopkins. We used oocytes from the frog *Xenopus laevis*. This convenient expression system was particularly useful, since frog oocytes have very low water permeability and survive even in fresh water ponds. Control oocytes were injected with water alone; test oocytes were injected with 2 ng of cRNA encoding our protein. After three days of protein synthesis, the oocytes appeared essentially identical. Then we stressed the oocytes by transferring them to distilled water, and an amazing difference was immediately apparent. Having exceedingly low water permeability, the control oocytes failed to swell. In contrast, the test oocytes were highly permeable to water and exploded like popcorn [Fig. 2] (Preston et al., 1992). This result produced much celebration in the laboratory; the celebrations continue still. The protein was christened "aquaporin" and is now officially designated "AQP1", the first functionally defined water channel protein (Agre et al., 1993b). We confirmed the function of this protein by studying the purified AQP1..." ===== "In science, one should use all available resources to solve difficult problems. One of our most powerful

resources is the insight of our colleagues. I spoke to a dozen or more well--known biochemists and physiologists about this protein, but none could predict what its function might be. My clinical mentor, John C. Parker (1935--1993) at the University of North Carolina at Chapel Hill, was the first to suggest to me that red cells and renal tubules were exceedingly permeable to water. He recommended that we consider a role in membrane water transport. While John did not live to see our later studies, he did live to see our initial discovery and we celebrated together." The remainder of this Nobel lecture freely available on line has very exciting `stuff', presented in a clear and accessible manner by the 2003 Nobel Laureate Peter Agre and covers much more than his group's outstanding and most surprising findings, including the detailed molecular structure of aquaporin-1, as well as a discussion of the medical relevance of other aquaporins (perhaps, with more Swedish prizes to be awarded to some of those in the years to come ?)

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